REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim Amendments

Claims 1, 3-7, and 13-16 were pending in this application. Claims 2 and 8-12 were previously canceled without prejudice or disclaimer. Claim 5 is cancelled herein without prejudice or disclaimer.

Claims 1, 3-4, and 15-16 are amended. Claim 1 is amended to recite a blister pack for pharmaceutical use comprising blisters containing a compressed "granulate" tablet comprising desmopressin, or a pharmaceutically acceptable salt thereof and an "acid" that provides a pH in the range of from 3.0 to 6.2 as measured when 1 g of the tablet is slurried in 2 ml of water at 25°C. No new matter is introduced by the amendment. Support for the amendments can be found throughout the application as filed, for example, in page 6, lines 8-10, and Example 1 for the recitation of a compressed "granulate" tablet, and in original claim 5 and at page 4, lines 14-19, of the application as filed, for the recitation of an "acid."

Claims 3, 4, 15, and 16 are amended to correct claim dependency and antecedent basis.

The cancellations and/or amendments are made without prejudice or disclaimer. Applicants reserve the right to pursue any canceled subject matter in one or more continuing application(s) with the same rights of priority as the instant application.

New claim 17 is added. No new matter is introduced by the new claim. Support for new claim 17 can be found, for example, at page 4, lines 16-19 of the application as filed.

After amending the claims as set forth above, claims 1, 3-4, 6-7, and 13-17 will be pending. These claims are presented for reconsideration.

Withdrawn Objections/Rejections

Applicant notes with appreciation the Office's withdrawal of the objection to the specification; rejection of claims 1, 3-7, 13, and 14 under 35 U.S.C. §112, second paragraph; rejection of claims 1 and 6 under 35 U.S.C. §102(b) as being allegedly anticipated by

Minirin®; rejection of claims 1, 3-5, 7, and 13 under 35 U.S.C. §102(b) as being allegedly anticipated by Flockhart; and rejection of claims 1, 3-7, 13, and 14 under 35 U.S.C. §103(a) as being allegedly anticipated by Flockhart in view of Nilsson.

New Claim Objection

Claim 3 is objected to under 37 C.F.R. §1.75(c), as being of improper dependent form for failing to further limit the subject matter of the previous claim. Applicant thanks the Office for pointing out the typographical error in claim 3, which is amended above to correct the error, thereby obviating the objection.

New Claim Rejections under 35 U.S.C. §112, first paragraph

Claims 1 and 5 stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. In particular, the Office alleges that the specification does not enable the full scope of the claims with respect to the recited "agent" (claim 1) or "acid" (claim 5). Applicant respectfully disagrees.

Without acquiescing to the merits of this rejection, and solely to advance prosecution, claim 1 is amended to replace the term "agent" with the term "acid" as previously recited in claim 5, and claim 5 is canceled. As reflected in amended claim 1, the acid provides a pH in the range of from 3.0 to 6.2 as measured when 1 g of the recited tablet is slurried in 2 ml of water at 25°C. Suitable such acids are exemplified in the specification as citric acid, hydrochloric acid, malic acid, stearic acid, acetic acid, phosphoric acid, adipic acid, tartaric acid, glutamic acid, and aspartic acid. Specification, page 4, lines 14-19. Moreover, Examples 1 and 4 of the specification provide working examples of a compressed granulate tablet containing desmopressin and malic acid. Therefore, the specification provides ample guidance to permit a skilled artisan to select a suitable acid without any undue amount of experimentation.

The §112 rejection appears to be based on the mere breadth of the term "acid," but breadth alone does not undermine enablement. The purpose of the acid is to provide a pH within the recited range, and the Office does not explain why a skilled artisan would not be able to select a suitable acid for that purpose without an undue amount of experimentation. The fact that the skilled artisan could chose between a large number of acids in no way

undermines enablement, as long as the selection can be made without an undue amount of experimentation. However, the Office provides no scientific reasoning or other basis whatsoever for the assertion that "one of ordinary skill in the art would be faced with an undue experimental burden in attempting to practice the invention." Office Action, pg. 5-6.

As set forth in MPEP § 2164.04, "[i]n order to make a rejection, the ***examiner*** has the initial burden to establish ***a reasonable basis*** to question the enablement provided for the claimed invention" (emphasis added). Where, as here, the "specification disclosure . . . contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented ***must be taken as being in compliance with the enablement requirement . . . unless there is a reason*** to doubt the objective truth of the statements contained therein" (emphasis added). Here, where no such reason has been put forward, the rejection is improper and should be withdrawn.

Applicant also vehemently disagrees with the assertion that "the instant invention is seemingly concerned with an extremely limited subclass of agents and acids." Again, the Office provides no basis whatsoever for this assertion. Indeed, because the claims reflect that which the Applicant contemplates to be the invention, the broad terms used in the claims underscore the breadth of the invention with regard to the pH adjusting agent. The fact that the specification does not list every possible acid does not limit the scope of the invention, but rather reflects the realties of patent application drafting, and the guidance that what is well-known in the art is best omitted from the description. *See In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

For at least the foregoing reasons, Applicant urges reconsideration and withdrawal of the enablement rejections.

Claim Rejections under 35 U.S.C. §103(a)

Claims 1, 3-7, and 13-16 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Fein (US Publication No. 2004/0138098). Applicant respectfully traverses.

As reflected in independent claim 1, the instant claims are directed to a blister pack for pharmaceutical use comprising blisters containing a compressed granulate tablet which

tablet comprises: desmopressin, or a pharmaceutically acceptable salt thereof; an acid that provides a pH in the range of from 3.0 to 6.2 as measured when 1 g of said tablet is slurried in 2 ml of water at 25°C; and a pharmaceutically acceptable adjuvant, diluent or carrier. Fein does not teach or suggest a blister pack comprising such a compressed granulate tablet.

Fein is directed to orodispersible forms of desmopressin which are absorbed directly from the mouth, instead of being swallowed. Fein's tablets are ***not*** compressed granulate tablets as recited in the instant claims, but rather are fast-dissolving tablets formed by direct compression of a mixture of the materials. *See, e.g.* Fein, page 5, paragraphs [0055] – [0058]. Indeed, Fein's goal of rapid dissolution in the mouth is inconsistent with compressed granulate tablets. This is seen in Comparative Examples 2 and 3 of Fein, which describe granulate tablets in contrast to Fein's tablets. Thus, at its most fundamental level, Fein is not related to the dosage forms recited in the instant claims.

Additionally, Fein does not teach or suggest the use of an acid in a compressed granulate tablet with desmopressin where the acid provides a pH in the range of from 3.0 to 6.2 when 1 g of the tablet is slurried in 2 ml of water, as recited in the instant claims. Fein mentions the use of an acid source in combination with a carbon dioxide source, such as alkaline carbonate or bicarbonate, to make the effervescent agent that evolves gas (see Feind, page 5, paragraph [0061]), but this teaching does not suggest the use of an acid to provide a pH as claimed. Indeed, Fein teaches the use of an acid source in conjunction with a the carbon dioxide source, preferably in equivalent ratios. *See, e.g.*, Fein, page 5, paragraph [0062]. Slurrying such a tablet in water would promote reaction between the acid and effervescent agent, resulting in consumption of the acid, not the provision of a desired pH, as claimed.

The Office also cites Fein's teaching to use a pH adjusting agent to adjust the pH of a solution from which the dosage form is prepared. *See, e.g.*, Fein, pages 7-8, paragraph [0091]. However, these teachings are provided in the context of a different embodiment of Fein, not its compressed tablets. Rather, these teachings relate to embodiments where the dosage form comprises an open matrix network carrying desmopressin that is made by a freeze-drying or sublimation process. *See, e.g.*, Fein, pages 6-8, paragraphs [0074] – [0098]. It is only in this context that Fein teaches the use of a pH adjusting agent to control the pH of

the solution subject to the freeze-drying or sublimation process. Thus, this teaching does not suggest the present invention, which relates to the use of an acid to provide a pH in a target range when a compressed granulate tablet is slurried in 2 ml of water.

Finally, Applicant emphasizes that Fein discloses blister packaging only in connection with the preparation of a freeze-dried product which is not a compressed tablet of any kind. *See, e.g.*, Fein, page 8, paragraphs [0092] and [0093]. Indeed, Examples 1-6 on page 10 of Fein illustrate the use of blister packaging for the storage of freeze dried product only. In contrast, Fein expressly teaches storing its compressed tablets in bulk, *i.e.*, not in a blister pack. *See, e.g.*, Fein, page 3, paragraph [0040].

While the Office might assume that any dosage form of desmopressin can be packaged in any manner, such an assumption ignores the state of the art with regard to desmopressin. As noted in paragraph [0004] of the instant specification, the desmopressin acetate tablet product Minirin® was marketed in a blister pack, but the blister pack product was withdrawn from the market in 2002 due to a consistent problem with degradation of the desmopressin acetate during long term storage. Knowing of this problem, the skilled artisan would have been discouraged from packaging desmopressin ***tablets*** in blister packs, and Fein's teaching to package ***freeze dried*** dosage forms in blister packs would not have convinced them otherwise.

In summary, although the Office Action attempts to make out a case of obviousness by picking, choosing and combining isolated teachings relating to distinct embodiments of Fein, the skilled artisan reading Fein without the benefit of the instant disclosure would find no suggestion of the present invention, including no suggestion to package a compressed granulate tablet comprising desmopressin in blister packaging, and no suggestion to use an acid as claimed to provide a pH range as claimed. Thus, Applicant respectfully urges reconsideration and withdrawal of the §103 rejection based on Fein.

Indeed, the obviousness rejection overlooks the contribution of the invention over the state of the art in providing a form of desmopressin that can be packaged in blister packs without suffering from degradation. As taught in the specification, it was surprisingly discovered that the claimed compressed granulate tablets show unexpected stability when stored in blister packs. For example, paragraph [0011] teaches that "it has been found that a

purposive selection and control of the pH level in a solid dosage form of desmopressin is particularly efficient in counteracting degradation upon storage in blister packs." The unexpected results are illustrated, for example, in Example 3 (PVC blister) and Example 4 (PVC/PVDC blister) at pages 7-8 of the specification, which compare the degradation of desmopressin (upon storage) with respect to compressed granulate tablets with and without an acid as recited in the pending claims. Example 3 demonstrates that the tablet with acid retains 76% of its desmopressin after 7 months of storage as compared to only 52% remaining in the tablet with no acid. Similarly, Example 4 demonstrates that the tablet with acid retains 82% of its desmopressin after 6 months of storage as compared to 76% of desmopressin in the tablet with no acid. Thus, the present invention solves a significant problem faced by the art, and provides a solution that is not taught or suggested by Fein.

CONCLUSION

Applicant believes that the present application is in condition for allowance. Favorable reconsideration of the application is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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